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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/058,903	01/28/2002	Timothy Robert Hurley	A0000513-01-DRK	7220

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EXAMINER	
KHARE, DEVESH	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/058,903	HURLEY ET AL.	
	Examiner	Art Unit	
	Devesh Khare	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03/05/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The remarks and arguments filed on 12/19/2003 are acknowledged. Claims 1- 7 are currently pending in this application.

35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pande (U.S. Patent 6,359,005) in view of Wirth et al. (J. Pharm. Sci.,87(1), 31-39, 1998) of record.

The **claims 1-4** are directed to pregabalin lactose conjugates, or a pharmaceutically acceptable salt, ester, amide, and prodrug thereof. Additional claim limitations claimed include a pharmaceutical formulation comprising at least one compound of pregabalin lactose conjugate and a pharmaceutically acceptable carrier, excipient, or diluent thereof; and applicant has elected the hexose-hexose group in the pregabalin conjugate in claims 2 and 3.

Pande teaches the pregabalin, its derivatives, and pharmaceutically acceptable salts for use in the treatment of mania and bipolar disorder (see abstract). In column 3, lines 14-17, the pharmaceutical compositions of pregabalin or its salts with a pharmaceutically acceptable carrier are disclosed. Pande also discloses a

pharmaceutical composition of pregabalin comprising a pharmaceutical carrier such as lactose (col. 3, lines 22-24). In column 2, a line 47-54, the use of pregabalin in the treatment of patients suffering from anxiety is disclosed. In column 3, lines 63-67, the use of pregabalin in the treatment of patients suffering bipolar disorder especially the epilepsy is disclosed. Pande also disclose suitable pharmaceutical carriers; including the pharmaceutical diluent lactose (see col. 3, 22-24). While the Pande's use of pregabalin and derivatives in the treatment of anxiety or epilepsy use closely analogous compounds to the applicant's compounds, Pande's pregabalin compounds and compositions differ from applicant's pregabalin lactose conjugates and compositions in that the pregabalin compounds are not conjugated with lactose.

Wirth et al. teach drugs which are secondary amines undergo the Maillard reaction with lactose and lactose is used as the most common excipient in the formulations of fluoxetine HCl (see abstract). Applicants in example 5 disclose that the pregabalin undergoes a Maillard reaction to form conjugates with lactose in formulated product. Wirth et al, discloses that the Maillard reaction of secondary amines and lactose should be considered when selecting formulation ingredients and when examining the stability of such products" (page 38, last para.). Wirth et al. disclose that the reducing carbohydrate such as lactose is substrate for the Maillard reaction (see page 31, bottom of first col. and scheme 2 on page 33). Wirth et al. disclose that the lactose is widely used as diluent for capsules and tablets due to its low price, high purity, and excellent compression and stability characteristics and its ability to undergo Maillard reactions to produce formulation (see page 31, sec. col., sec. para). It is noted

that Wirth et al. does not provide specific disclosures regarding the pregabalin lactose conjugate.

Therefore, one of ordinary skill in the art would have found the applicants claimed pregabalin lactose conjugates and their pharmaceutical formulation to have been obvious at the time the invention was made having the above cited references before him. Since Pande teaches the pregabalin, its derivatives, and pharmaceutically acceptable salts for use in the treatment of anxiety or epilepsy (nervous system disorder), and Wirth et al., teach the excellent compression and stability characteristics of lactose and its ability to undergo Maillard reactions to produce formulation, one skilled in the art would have a reasonable expectation for success in combining the teachings of both references to obtain a pregabalin lactose conjugate and its pharmaceutical composition. The motivation for doing so is provided by Pande, which suggests the use of pregabalin in the treatment of anxiety or epilepsy because of the nontoxic nature of the compound, ease of preparation and the ease of administration of the drug (see col. 3, lines 55-60).

Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pande (U.S. Patent 6,359,005) in view of Wirth et al. (J. Pharm. Sci.,87(1), 31-39, 1998) of record.

The **claims 5-7** are directed to a method for treating a subject having a central nervous system disorder or disease by administering to the subject a pharmaceutically

effective amount of a compound of claim 1 (pregabalin lactose conjugates, their pharmaceutical formulation). Additional claim limitations include the central nervous system disorder or disease selected from depression, seizure, anxiety, pain, sleep disorder, consumptive disorder, psychosis, dyskinesia, Huntington's disease, or Parkinson's disease; and applicant has elected the hexose-hexose group in the pregabalin conjugate in claim 5.

Pande teaches the pregabalin, its derivatives, and pharmaceutically acceptable salts for use in the treatment of mania and bipolar disorder (see abstract). In column 3, lines 14-17, the pharmaceutical compositions of pregabalin or its salts with a pharmaceutically acceptable carrier are disclosed. Pande also discloses a pharmaceutical composition of pregabalin comprising a pharmaceutical carrier such as lactose (col. 3, lines 22-24). In column 2, a line 47-54, the use of pregabalin in the treatment of patients suffering from anxiety is disclosed. In column 3, lines 63-67, the use of pregabalin in the treatment of patients suffering bipolar disorder especially the epilepsy is disclosed. Pande also disclose suitable pharmaceutical carriers; including the pharmaceutical diluent lactose (see col. 3, 22-24). While the Pande's use of pregabalin and derivatives in the treatment of anxiety or epilepsy use closely analogous compounds to the applicant's compounds, Pande's pregabalin compounds and compositions differ from applicant's pregabalin lactose conjugates and compositions in that the pregabalin compounds are not conjugated with lactose.

Wirth et al. teach drugs which are secondary amines undergo the Maillard reaction with lactose and lactose is used as the most common excipient in the

formulations of fluoxetine HCl (see abstract). Applicants in example 5 disclose that the pregabalin undergoes a Maillard reaction to form conjugates with lactose in formulated product. Wirth et al, discloses that the Maillard reaction of secondary amines and lactose should be considered when selecting formulation ingredients and when examining the stability of such products" (page 38, last para.). Wirth et al. disclose that the reducing carbohydrate such as lactose is substrate for the Maillard reaction (see page 31, bottom of first col. and scheme 2 on page 33). Wirth et al. disclose that the lactose is widely used as diluent for capsules and tablets due to its low price, high purity, and excellent compression and stability characteristics and its ability to undergo Maillard reactions to produce formulation (see page 31, sec. col., sec. para). It is noted that Wirth et al. does not provide specific disclosures regarding the pregabalin lactose conjugate.

Therefore, one of ordinary skill in the art would have found the applicants claimed method for treating a subject having a central nervous system disorder or disease by administering to the subject a pharmaceutically effective amount of pregabalin lactose conjugates, to have been obvious at the time the invention was made having the above cited references before him. Since Pande teaches the pregabalin, its derivatives, and pharmaceutically acceptable salts for use in the treatment of anxiety or epilepsy (nervous system disorder), and Wirth et al., teach the excellent compression and stability characteristics of lactose and its ability to undergo Maillard reactions to produce formulation, one skilled in the art would have a reasonable expectation for success in

combining the teachings of both references to accomplish the pregabalin lactose conjugate, its pharmaceutical composition and their use in the treatment of anxiety or epilepsy. The motivation for doing so is provided by Pande, which suggests the use of pregabalin in the treatment of anxiety or epilepsy because of the nontoxic nature of the compound, ease of preparation and the ease of administration of the drug (see col. 3, lines 55-60).

Rejection Maintained

Rejection of claims 1-7 under 35 U.S.C. 103(a) is maintained for the reasons of record.

Response to Arguments

Applicant's arguments filed on 12/19/03 traversing the rejection of claims 1-7 under 35 U.S.C 103(a) have been fully considered but they are not persuasive.

Applicants argue that "the claimed compounds are not taught or suggested by the reference"; "there is no basis in either reference itself for combining them"; and neither reference provides motivation to combine the references". It is noted that applicant has elected the hexose-hexose group in the pregabalin conjugate compounds. Pande teaches a pharmaceutical composition comprising pregabalin and lactose (col. 3, lines 22-24). Wirth et al. teach drugs which are secondary amines undergo the Maillard reaction with lactose (abstract) and the Maillard reaction of secondary amines and lactose should be considered when selecting formulation ingredients and when examining the stability of such products" (page 38, last para.). Indeed, the examiner has established a prima facie case of obviousness rendering claims 1-7 rejected under

35 U.S.C. 103(a) by addressing sufficiently all of the limitations set forth in the instant claims, one skilled in the art would have a reasonable expectation for success in combining the above said references to accomplish a pregabalin lactose conjugate and its pharmaceutical composition in the treatment of anxiety or epilepsy because of the nontoxic nature of the compound, ease of preparation and the ease of administration of the drug (see col. 3, lines 55-60).

2. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the

Examiner should be directed to Devesh Khare whose telephone number is (703)605-

1199. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, Supervisory Patent Examiner, Art Unit 1623 can be reached at 703-308-4624. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Devesh Khare, Ph.D.,J.D.
Art Unit 1623
May 20,2004